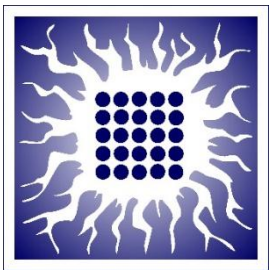

“Vinca” Institute of Nuclear Sciences

MAGBIOVIN project

Conference: **"Magnetic nanoparticles and their applications in medicine"**

Date: April 4-5, 2019.

Venue: Rectorate of the University of Belgrade, Studentski Trg 1, Belgrade

Conference organizer: Project MAGBIOVIN, “Vinca” Institute of Nuclear Sciences

Conference organizing committee

Bratislav Antic, Magbiovin project coordinator
ZeljkoPrijovic, Era Chair Magbiovin project
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Project MAGBIOVIN

The MAGBIOVIN project is focused on the development of novel magnetic nanomaterials designed for biomedical applications, as a basis for new tumor therapies. Their antitumor effect is based on the ability of nanoparticles to spontaneously accumulate or to be driven into tumor by the magnets, and when exposed to an oscillatory magnetic field they release heat (magnetic hyperthermia). With the addition of certain radionuclides that destroy the tumor by radiation or drugs that are targeted releasing into tumor by the magnetic field, an increased localized antitumor effect that saves healthy tissue is obtained. To this goal, the human tumor cell lines are being investigated, and within the Center of Excellence, the "Vinca" Institute has formed a mice vivarium without immune systems on which human tumors are grown, as the best testing model for the effectiveness of new methods.

The MAGBIOVIN project is funded by the European Commission within the framework of the FP7-EraChair Call-2013, and it is implemented in the 2014-2019 period.

Conference Scope

In the last decade the synergistic research between nanotechnology, materials science and medicine demonstrated the great potential of interdisciplinary science. We have witnessed important advances in what is now known as Nanomedicine, comprising many non-invasive, highly specific diagnostics tools and therapies. The programme of the "Magnetic nanoparticles and their applications in medicine" conference comprises sessions from several application domains of nanotechnology, and it focuses on innovations in materials and their clinical applications. To meet the challenges of a fast-evolving field as Nanomedicine, we have gathered prominent scientists with most active contributions to their respective fields, which we are sure, will result in a remarkable opportunity for the audience to get a first-hand overview of the latest developments in nanomaterials and nanomedicine.

It is the wish of the Organizing Committee that the meeting also provide an excellent opportunity to foster existing collaborations and to establish new contacts among our colleagues.

We wish the MAGBIOVIN Conference much success. May all participants enjoy this exchange of ideas and have a vivid and exciting time at the conference.

Conference program

Thursday, 4th April

09:30-09:45 **Conference Opening**

09:45-10:25 Quentin A. Pankhurst, *"Biomedical Applications of Radionuclide-Labelled Magnetic Nanoparticles"*

10:25-11:05 Robert Ivkov, *"The tumor immune microenvironment is reshaped after systemic exposure to magnetic iron oxide nanoparticles: A study in mouse models of breast cancer"*

11:05-11:40 **Coffee break**

11:40-12:10 Florence Gazeau, *"Long term fate of iron oxide nanoparticles in the body: a long and comprehensive survey"*

12:10-13:00 Adriele Prina-Mello, *"Translational requirements for nanotechnology enable medical products"*

13:00-15:00 **Lunch**

15:00-15:40 Holger Grüll, *"Nanoparticles for Molecular Imaging and Therapy"*

15:40-16:20 Olivier Sandre, *"Monocore or multicore iron oxide nanoparticles synthesized in polyols and coated with a thermosensitive cell-penetrating peptide"*

16:20-16:40 **Coffee break**

16:40-17:20 Željko Prijović, *"Magnetic nanomaterial as a mediator, carrier and trigger for hyperthermia-complementing combined therapies of tumors: MagBioVin approach"*

17:20-18:00 María del Puerto Morales,*"Magnetic nanoparticles aggregation effects on cellular magnetic hyperthermia"*

Friday, 5th April

09:45-10:25 Sanjay Mathur, *"Chemically Engineered Iron Oxide Nanocrystals for Transport of Biomolecules Across Biological Barriers"*

10:25-11:05 Vittoria Raffa, *"Mecanotransduction of axonal growth: a new strategy based on magnetic nanoparticle to remote nerve regeneration"*

11:05-11:40 **Coffee break**

11:40-12:10 Boris Polyak, *"Nanomagnetic approaches for vascular healing and cardiac regeneration"*

12:10-13:00 Ana Espinosa, *"Thermal therapies mediated by iron oxide-based nanoparticles: quantitative comparison of heat generation, therapeutic efficiency and limitations"*

13:00-15:00 **Lunch**

15:00-15:40 Gerardo F. Goya, *"On the feasibility of improving heat production in magnetic fluid hyperthermia: the time of topology"*

15:40-16:20 Giuseppe Cirillo, *"Graphene oxide functional nanohybrids with magnetic nanoparticles for improved vectorization of anticancer therapeutics"*

16:20-16:40 **Coffee break**

16:40-17:20 Victor Kuncser,*"Engineering and optimization of Specific Absorption Rates of Fe oxide nanoparticles in magnetic hyperthermia"*

17:20-18:00 David Serantes, *"Taking magnetic hyperthermia and magnetogenetics to the next level: key aspects to address from a basic-physics point of view"*

18:00 **Conference Closing**

ABSTRACTS

Biomedical Applications of Radionuclide-Labelled Magnetic Nanoparticles

Quentin A. Pankhurst

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'Healthcare Biomagnetics' – the sensing, moving and heating of magnetic nanoparticles *in vitro* or in the human body – offers the potential for safe and convenient alternatives for many therapeutic and diagnostic applications. This is leading to the development of products such as remote sensors, mechanical actuators, and therapeutic heat sources. In this lecture a selection of recent examples of this work will be presented and discussed, with a particular focus on applications involving the use of radionuclide-labelled magnetic nanoparticles.

Quentin Pankhurst

Professor Quentin Pankhurst is a Professor of Physics and Director of the Healthcare Biomagnetics Laboratory at University College London – one of the top universities in the UK, and consistently rated one of the top 20 higher education institutions in the world. Previously, in 2008, he was the Director of the Davy-Faraday Research Laboratory at the Royal Institution of Great Britain (in Mayfair, London), where he held a position once held by such luminaries as Michael Faraday and Ernest Rutherford. On his return to UCL in 2011, he set up the UCL Institute of Biomedical Engineering, a cross-faculty institute that brought together 250 PIs and their teams – more than a thousand researchers in total – in common programmes based on translational research and experimental medicine.

Quentin's work in bio- and nanomagnetism is directed towards making practical advances in the use of magnetic nanoparticles in healthcare. In his career to date he has published more than 250 papers that have been cited more than 13,500 times, and he has generated more than £45M in research grant income and investment. He is a co-inventor on 12 patent families with 80+ national filings covering applications in magnetic sensing, heating and actuation; and he is the co-founder of three spinout companies: Endomagnetics Ltd (Apr. 2007); Resonant Circuits Limited (Sept. 2009); and MediSieve Ltd (Apr. 2014). Together, these companies employ more than 25 full-time staff; and one of them, Endomagnetics Ltd, recorded an annual turnover in 2017/18 of more than £6.0M.

Quentin was born and raised in New Zealand, and has lived in England since 1983. He is married and has two daughters.

The tumor immune microenvironment is reshaped after systemic exposure to magnetic iron oxide nanoparticles: A study in mouse models of breast cancer

Preethi Korangath, James Barnett, Anirudh Sharma, Elizabeth Henderson, Jacqueline Stewart, Shu-Han Yu, Sri Kamal Kandala, Chun-Ting Yang, Mohammad Hedayati, Todd Armstrong, Elizabeth Jaffee, Cordula Gruettner, Xian C Zhou, Wei Fu, Chen Hu, Saraswati Sukumar, Brian W Simons and **Robert Ivkov**

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The factors that influence selective accumulation of nanoparticles into solid tumors remain an area of intense interest. Five tumorigenic human breast cancer cell lines with varying HER2 status were used to grow orthotopic mammary tumors in nude and NOD/SCID gamma (NSG) mice. A human HER2 overexpressing (huHER2) transgenic mouse (Genentech) was used to develop a syngeneic allograft model that was implanted across FVB/N (immune competent), nude, and NSG mice for comparative studies of tumor retention of nanoparticles. Starch-coated bionizednanoferrite (BNF) nanoparticles labeled with trastuzumab (BNF-HER), unlabeled (BNF-Plain), or PBS (control) were injected into tail veins of mice when tumors had a measured volume of ~150 mm^3. 24 hrs following intravenous injection, mice were sacrificed and tissues harvested for analysis.

We demonstrate using inductively coupled plasma mass spectrometry and extensive histophathology analysis that unlabeled starch-coated magnetic iron oxide nanoparticles showed little accumulation in tumors regardless of tumor model or host strain. Surprisingly, retention of BNF-HER nanoparticles was evident across all tumor models, with little variation among the models. Further analysis showed that retention of the antibody-labeled counterpart in tumors depended more on immune status of the host than on presence of the target antigen.

In vitro, a T_H1-type activation of murine macrophages and neutrophils led to preferential uptake of antibody-conjugated nanoparticles, suggesting nanoparticle retention in tumors was determined by an inflammatory tumor-microenvironment. In the immune competent huHER2 allograft model, accumulation of plain nanoparticles was minimal as observed in human xenograft models. Conversely, retention of BNF-HER nanoparticles in FVB/N mice bearing huHER2 tumors was dramatically higher than in nude or NSG mice bearing this tumor, with tumor retention occurring primarily in tumor-associated dendritic cells, neutrophils, monocytes, and macrophages as determined by magnetically sorted flow cytometry. An intact immune system with competent T_H1 activation displayed preferential retention of antibody-labeled BNF nanoparticles.

Systemic exposure of immune intact allograft (implanted) huHER2 models to either plain or trastuzumab-labeled BNF nanoparticles delayed tumor growth and caused $CD8^+$ T cell infiltration fourteen days after injection.

These findings demonstrate that the immune microenvironment of solid-cancer tumors can be a dominant factor that determines nanoparticle retention in tumors, and that systemic exposure to nanoparticles has potential to initiate systemic immune responses leading to adaptive immune-mediated tumor growth inhibition.

Our results show that nanoparticle constructs offer anti-cancer immune-modulating potential that can be exploited for cancer immune therapy.

Robert Ivkov

Dr. Robert Ivkov is an assistant professor of radiation oncology and molecular radiation sciences and oncology at the Johns Hopkins University School of Medicine. His research interests include the development, characterization, and use of nanomaterials to target cancer and to enhance the effectiveness of current therapies such as radiation. He has a particular focus of selective heating with magnetic nanoparticles. Dr. Ivkov earned his M.D. and Ph.D. in physical chemistry from the University of Maryland and his M.Sc. from the University of Toronto, with an emphasis on thermodynamic properties of proteins. He continued to perform basic materials research at the National Institute of Standards and Technology, and later moved to the private sector to develop oncology products. Prior to his arrival to Johns Hopkins, Dr. Ivkov was vice president of research and development and a co-founder of Triton BioSystems, Inc., a company developing targeted nanotherapeutics for oncology.

Long term fate of iron oxide nanoparticles in the body: a long and comprehensive survey

Florence Gazeau

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Iron oxide nanoparticles (IONPs) are among the most promising nanomaterials in biomedicine mostly due to their unique magnetic properties but also to their biocompatibility and degradability. However, some questions remain on their long-term fate and biotransformation in the organism. How long will the nanoparticles keep their magnetic properties and be useful for applications? Where does the degradation take place? What are the mechanisms? What is the fate of degradation products? Is there any recycling and transfer between organs? What is the journey of the different particle components, the core and the shell? Which biological response/adaptation to IONP overload and degradation?
I will present some of our latest results regarding the fate of different types of IONP in mice.
A part of my talk will focus on a possible pathway for metabolizing IONP degradation products through a protein involved in iron metabolism, the ferritin. We have studied, in solution, the degradation processes of iron oxide nanoparticles in the presence of ferritin proteins as well as the iron transfer processes from nanoparticles to ferritin. The difficulty is the high concentration of endogenous iron which makes it impossible to demonstrate such transfers *in vivo*. Thus, we have developed a strategy to track these phenomena *in vivo* by doping iron oxide nanoparticles with a scarce element in the organism, such as cobalt. This work highlighted a possible mechanism of biological recycling, remediation and detoxification of metal oxide nanoparticles mediated by endogenous proteins at the molecular scale. We also developed a multi-scale method to study the life cycle of iron oxide nanoparticles and their by-products in the organism. The main challenge is to differentiate iron steming from the nanoparticles from endogeneous iron. This specific tracking problem is routinely encountered in geochemical studies and solved by labelling the target material with minor stable isotopes. Therefore, iron oxide nanoparticles enriched in the minor stable isotope ^{57}Fe were synthetised and injected intravenously in mice to follow dynamic circulations of iron oxide nanoparticles and their by-products over a period of six months. We have also labelled the particle coating to track the integrity of nanoparticles over time and decipher the specific fates of inorganic core and organic shell. Results of this comprehensive in vivo study will be discussed together with modifications of gene expression related to the presence, accumulation and degradation of IONPs at different doses and in different organs. Comparison with different types of materials, e.g. gold nanoparticles, will be highlighted.

Florence Gazeau

Florence Gazeau, PhD in Physics 1997, University Paris Diderot, is senior scientist in CNRS. PI of the Biother group (http://biother.net), she is recognized in the domain of nanomagnetism and nanomedicine. Her research interests include imaging and therapeutic applications of activable nanoparticles, nanotoxicity, life-cycle and long-term fate of nanoparticles, mechanobiology of cancer, regenerative medicine and extracellular vesicles for regenerative medicine and drug delivery. She is deputy director of the laboratory Matière et Systèmes Complexes (MSC) at USPC (Université Paris Diderot/CNRS) and one of the leaders for the creation of MSC Med laboratory (Université de Paris 2019). She is author of more than 136 publications (h-index of 46, citations >7500), inventor of 6 pending patents and cofounder of EverZom start up for the production of Extracellular Vesicles.

Translational requirements for nanotechnology enable medical products

Adriele Prina-Mello[1,2,3]

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[2] *Laboratory for Biological Characterisation of Advance Materials (LBCAM) and Nanomedicine Group, Trinity Translational Medicine Institute, Trinity College Dublin, Dublin 8, Ireland*
[3] *Centre for Research on Adaptive Nanostructures and Nanodevices (CRANN) Institute and AMBER Centre, Trinity College Dublin, College Green, Dublin 2, Ireland*

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Pre-clinical assessment of nanomaterial is a key process for nanotechnology enabled medical products. To maximise effort and costs, a successful multiparametric pre-clinical assessment cascade is needed. Consideration for similarities between the pre-clinical and clinical screening are draw up assessing industrially relevant aspects such as safe- and quality- by-design across the critical steps that lead to product market approval. Starting from the physical and chemical characterisation, to the specific theranostics properties, SuperParamagnetic Iron Oxide Nano Particles (SPIONS) are presented as one of the most promising theranostic nanomaterial for clinical application. Thus, the use of screening platforms, based on cell-nanoparticle mechanism of biological interaction, are introduced for cost-effective go/no go assessment; these comprising sterility, endotoxicity, cytotoxicity, and immunotoxicity. In vivo testing strategies, for specific theranostic applications, are fundamental during the translational process. Finally, consideration on past and present clinically translated products highlights the importance in developing multiparametric pre-clinical experimental testing strategies focused on achieving sounds and robust dataset for clinical translation.

Adriele Prina-Mello

Dr Adriele Prina-Mello is currently working as ussher Assistant Professor in Translational Nanomedicine at Trinity College Dublin, University of Dublin and part of the League of Universities (LERU). His track-record in nanomedicine products translation from bench to bedsite, and expert in R&D and scientific regulatory aspects associated with nanotechnology-driven products. Key achievements of Dr Prina-Mello are: Director of the LBCAM (Laboratory for Biological Characterization for Advance Materials Director), aimed at developing clinically and industrially interdisciplinary R&D in the Biomedical and Healthcare area. He is also principal Investigator at AMBER centre (Advanced Materials and BioEngineering Research Centre) and CRANN institute (Trinity Nanoscience) European Technology Platform for Nanomedicine Executive Board member and (2017-2019) Chair of the Education and Training working group, former chair of Characterization and Toxicology group (2015-2017). European Commission Expert in Characterization/Member of the European Materials Characterization Council. His scientific interests are: Focused on advanced technology and materials translational research in NanoMedicine (*in vitro*/*in vivo* diagnostic, imaging and therapeutics), Theranostics, Lab-on-a-

chip, Medical devices and Tissue engineering applications. Industrial and EC Track Record: Member of several initiatives and association focused on the safe development of Translation of Medicines and their industrialization. Since 2011 assisted translation of 6 technology platforms from bench to bedside. Dr Adriele Prina-Mello was involved in several EC-H2020 and FP7 projects among these EU-NCL, REFINE, BIORIMA, NoCanTher, AMCARE, MULTIFUN, NAMDIATREAM and others. Scientific Track Record: *h*-index: 29; citations:2787, author of more than 100 peer-reviewed works, 8 book chapters, Associated Editorial Member of Precision Nanomedicine, Scientific Reports and Cancer Nanotechnology (Springer-Nature Publishing). To date delivered more than 50 keynote presentations in Nanotechnology for Medicine.

Nanoparticles for Molecular Imaging and Therapy

Holger Grüll

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Nanomedicine, the application of nanotechnology to healthcare, offers new clinical solutions in medical imaging and therapeutic applications. New nanomedicine material concepts allow the design of more powerful, multipotent agents of sizes ranging from nanometers to microns, with new properties and functionalities. These multi-potent particles will serve for example applications as contrast agents in medical imaging for improved in-vivo diagnostic or enable new applications such as spectral CT or magnetic particle imaging or ultrasound triggered local drug delivery at the site of disease. A prerequisite are multifunctional nanoparticles that are tailored towards their application but also take biological requirements into account.

In this presentation, some basic aspects of in vivo behavior of nanoparticles are discussed with respect to biodistribution, excretion pathways and biological barriers they have to overcome. As an example, work related to nanoparticles for CT imaging as well as magnetic nanoparticles for magnetic particle imaging will be presented. Finally, an outlook will be given with respect to application and medical approval of nanoparticles in medicine.

Holger Grüll

Holger Grüll studied chemistry in Cologne, Germany, and gained 1996 his PhD in Physical Chemistry. After his PhD, he was working several years as postdoc and guest researcher at the Ben-Gurion University of the Negev, Beer Sheva (Israel), the National Institute of Standards and Technology (NIST) in Gaithersburg (USA), and again the Ben-Gurion University of the Negev working on polymers, nanoparticles, biomimetic membranes and drug delivery systems. In 2000, he started his career at the Philips Research Laboratory in Eindhoven, The Netherlands, and became later responsible for the in vivo research on molecular imaging and therapeutic applications. In 2007, Dr. Grüll was appointed professor at the Eindhoven University of Technology holding a chair for Molecular Imaging and Image-guided Interventions. In 2016, Dr. Grüll received an appointment full professor at the department of radiology, University Hospital Cologne, where Dr. Grüll is heading the laboratory for experimental imaging. Main research areas are nanoparticles for imaging applications and drug delivery with main focus on high intensity focused ultrasound applications, temperature sensitive liposomes, magnetic nanoparticles and particles for spectral CT application in cancer.

Monocore or multicore iron oxide nanoparticles synthesized in polyols and coated with a thermosensitive cell-penetrating peptide

Olivier Sandre[1], Gauvin Hémery[1], Emmanuel Ibarboure[1], Elisabeth Garanger[1], Sébastien Lecommandoux[1], Pauline Jeanjean[2], Coralie Genevois[2], Franck Couillaud[2], Sabrina Lacomme[3], Etienne Gontier[3], Ashutosh Chilkoti[4]

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This communication reports the grafting onto iron oxide nanoparticles (IONPs) of recombinant polypeptides made of di-block elastin-like peptide (ELP_{40-60}) and cell-penetrating peptide (Tat) sequence.[1] The ELP_{40} block is thermosensitive and undergoes a water de-swelling transition at a critical temperature around 42 °C in solution, the ELP_{60} block is hydrophilic and provides colloidal stability to the resulting γ-Fe_2O_3@ELP_{40-60}-Tat core-shell IONPs. Magnetic IONPs were synthesized by a polyol pathway with either monocore (nanospheres) or multi-core (nanoflowers) morphology, narrow size-dispersity and suitable heating efficiency under an alternating magnetic field (AMF).[2] The bio-functionalization of these IONPs with the di-block ELP_{40-60}-Tat was achieved by a convergent strategy through strong coordination bonding of a phosphonate group introduced near the N-terminus of the polypeptide. To the best of our knowledge, this is the first report on a thermosensitive ELP_{m-n} polypeptide brush grafting onto magnetic IONPs. Large temperature variations of the sample (up to 30 °C) could be obtained in a few minutes by applying an AMF. Fast size changes of the magnetic core-thermosensitive shell nanoparticles were measured by *in situ* dynamic light-scattering (DLS) while the AMF was on. Variations of the hydrodynamic size were compared to the classical polymer brush model revised for the highly curved surface of nanoparticles. Cellular internalization and toxicity assays were performed on a glioblastoma (U87) human cancer cell line in view of applications for drug delivery activated magnetically. Superior cellular uptake was observed *in vitro* for multicore IONPs compared to monocore IONPs (for the same PEG coating),[3] and for IONPs@ELP_{40-60}-Tat peptide-grafted nanoparticles compared to IONPs@PEG controls prepared from the same (spherical) cores. The internalization pathway in lysosomes was monitored by electron microscopy on microtomes and confocal optical microscopy on live cells. Cellular toxicity after AMF application with these core-shell IONPs was ascribed to lysosomal membrane rupture and leakage into the cytosol. The intra-cellular fate of such IONPs, from their internalization to the effect of an AMF application, validates the use of thermosensitive peptide brushes on IONPs as drug delivery systems, addressing lysosomal compartments and triggering leakage of their content by external AMF application. Preliminary *in vivo* experiments evidenced the positive

[1] E Garanger, S MacEwan, O Sandre, A Brûlet, L Bataille, A Chilkoti, S Lecommandoux, *Macromol.* 2015, 48, 6617

[2] G Hemery, A Keyes, E Garaio, I Rodrigo, J A Garcia, F Plazaola, E Garanger, O Sandre, *Inorg. Chem.* 2017, 56, 8232

[3] G Hemery, C Genevois, F Couillaud, S Lacomme, E Gontier, E Ibarboure, S Lecommandoux, E Garanger, O Sandre, *Molecular Systems Design & Engineering* 2017, 2 629

effect of the Tat peptide end-sequence compared to the PEG brush control on the bio-distribution, with similar contents in the liver and in U87 model tumor in mice. Long term fate (after 48 h) is discussed in view of the cell division with equal sharing of the magnetically loaded lysosomes among daughter cells, possibly envisioning the successive application of magnetic hyperthermia on time scales superior to the cellular life cycle

Olivier Sandre

Dr Sandre Olivier is currently working as Senior CNRS researcher at LCPO Univ Bordeaux /Polymer self-assembly & life sciences. Dr. Olivier has defended PhD thesis of UPMC Université Paris 6 supervised by Pr. Françoise Brochard-Wyart at Curie Institute. He is member of advisory panel of IOP journal Nanotechnology and editorial board of MDPI Nanomaterials. Dr. Olivier received Young Researcher 2012 Award of the Chemical Physics. He is chair of CNRS Institute of Chemistry (2018-2023). Member (2013) and Chair (2017-) of Condensed Matter Division board of the French Physical Society (SFP), Member of RSC and Polymer Group GFP. Current research of Dr. Olivier is focused on: Magnetic nanoparticles (synthesis and properties); Polymer self-assemblies (micelles, vesicles…); Magnetically controlled drug release; Magnetic hyperthermia; MRI contrast agents.

Magnetic nanomaterial as a mediator, carrier and trigger for hyperthermia-complementing combined therapies of tumors: MagBioVin approach

Zeljko Prijovic

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Effective heating of the super-paramagnetic nanoparticles (MNPs) by alternating magnetic field (AMF) serves as a base for development of AMF-generated hyperthermia for tumor therapy. Despite being thoroughly investigated by years and the basic idea confirmed *in vitro*, it is sparsely used in clinics. The limitations arising from basic laws of physics, nature of the material and interaction with biological systems hamper the applicability *in vivo*. Namely, resembling some properties of viruses and bacteria, most of the MNPs encounter biological barriers and immune system components when applied *in vivo*, leaving relatively small amounts of MNPs capable of reaching the tumor. An opposite process, enhanced permeability and retention (EPR), allows MNPs to reach the tumor and retain there. However, it is frequently not sufficient to accumulate enough MNPs to effectively heat large volume of the tumor, hampering the use of therapy. Also, nature of MNP-mediated hyperthermia limits the cells damage to short distance only.

Combining our expertise in magnetism, radioisotopes, pharmacology and cancer biology in project MagBioVin, we focused on improving all phases of the approach, aiming to generate material and therapeutic approaches suitable for *in vivo* application. Aiming that goal, we have been optimizing the preparation of MNPs and their coating by various compounds (citrate, PEG, DOTA, dopamine, lysine etc…) to improves their circulation half-life, help avoiding immune system, lower the toxicity and serve as a linker for radioisotopes, drugs and bio-macromolecules. The produced material is screened for cytotoxicity and hyperthermia-induced cell death on mouse and human cancer cell lines *in vitro*. Material with suitable characteristic serves as a base for *in vivo* application.

Potential for tumor therapy of coated and derivatized MNPs have been tested *in vitro* measuring its impact on cancer cells in tissue culture and *in vivo* on the impact on growth of mouse and human tumor xenografts on immune-competent and immune compromised mice. The data confirmed the basic mode of action but facing the same limitations as reported earlier. To overcome them, we have been focused on developing combined therapies, by linking the MNPs to agents complementing or synergizing hyperthermia, as radionuclides (^{131}I, ^{90}Y, ^{177}Lu, ^{99m}Tc…), anticancer drugs (camptothecins), signal molecules (IL12), antibodies (CC49/Tag72) and enzymes (beta-Glucuronidase). The mechanism of action of the obtain material may have better pharmacological and therapeutic effects, surpassing hyperthermia alone, justifying their further development for eventual therapeutic approach.

Zeljko Prijovic

Dr Zeljko Prijovic received his PhD in biochemistry (medicinal enzymology) at School of Chemistry, University of Belgrade. Major focus of his work has been cancer research, more precisely development of low toxic therapies of tumors. His specialties are enzyme/prodrug therapies as Prodrug Monotherapy (PMT), Antibody-, Virus- and Bacteria-Directed Enzyme-Prodrug Therapies (ADEPT, VDEPT, BacDEPT), *in vitro* and *in vivo* tumor models including human tumor xenografts and orthotopic tumors. He has three patents regarding enzyme/prodrug therapy approaches and won two prizes for development of new technologies for pharmaceutical companies. After long-term engagement in Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan and School of Medicine, University of Patras, Greece, he is recently engaged in Nuclear Institute Vinca as ERA Chairperson on a project "Strengthening of the MagBioVin Research and Innovation Team for Development of Novel Approaches for Tumors Therapy based on Nanostructured Materials" (MagBioVin). Focus of the project is development of tumor therapies based on combination of magnetic nanomaterial, radioisotopes and biomolecules to overcome some of limitations of application of magnetic nanoparticles in oncothermia.

Magnetic nanoparticles aggregation effects on cellular magnetic hyperthermia

Maria Eugenia Fortes Brollo[1], Patricia Hernandez Flores[2], Lucía Gutiérrez[3], Domingo F. Barber[2] and **María del Puerto Morales**[1]

[1] *Department of Energy, Environment and Health, Institute of Material Science of Madrid (ICMM-CSIC), Madrid, Spain*
[2] *Department of Immunology and Oncology and Nanobiomedicine Initiative, Centro Nacional de Biotecnologıa, (CNB-CSIC), Madrid, Spain*
[3] *Department of Analytical Chemistry, Universidad de Zaragoza and CIBER-BBN, Instituto Universitario de Nanociencia de Aragon (INA), Zaragoza, Spain*
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Aggregation processes of magnetic nanoparticles in biosystems are responsible for alteration of their performance in vitro and in vivo due to the modification of their magnetic properties[1]. Here we present a systematic study using different nanoparticle coatings, cell lines, subcellular localizations, and nanoparticle core sizes, in an attempt to isolate the source of the high variability of the results obtained from different studies on cellular magnetic hyperthermia[2]. We have also developed models mimicking the aggregation degree and the spatial distribution of nanoparticles in biosystems (magnetoliposomes) and compare their magnetic properties with that of real biological examples (cells incubated with nanoparticles)[3]. The results indicate that the simple fact of being in contact with the cells makes the nanoparticles aggregate in a non-controlled way, which is not the same aggregation caused by the contact with the cell medium nor inside liposomes. These results could explain bibliographic data on the heating efficiency and MRI relaxivity changes for nanoparticles in contact with the cells.

María del Puerto Morales

María del Puerto Morales is Professor at the Institute of Material Science in Madrid (ICMM/CSIC), Spain since 2008. She got her degree in Chemistry by the University of Salamanca in 1989 and her PhD in Material Science from the Madrid Autonomous University in 1993. From 1994 to 1996, she worked as a postdoctoral fellow at the School of Electronic Engineering and Computer Systems of the University of Wales (UK) and got her permanent position at the ICMM/CSIC in 2000 (4 Sexenios). Her research activities are focused on the area of nanotechnology, in particular in the synthesis and characterization of magnetic nanoparticles for biomedicine, including the mechanism of particle formation,surface modification and its performance in biomolecule separation, NMR imaging, drug delivery and hyperthermia.

[1]Etheridge et al., Technology, **2(3)** (2014), 214-228
[2]Brollo, et al. Phys. Chem. Chem. Phys., **20** (2018) 17829-17838.
[3]Mejias et al., ACS Appl. Mater. Interfaces, **11(1)** (2019) pp 340–355

She has authored several book chapters in the field of nanoparticle synthesis (9), patents (3) and 200 articles in interactional scientific journals (h=51, >10.500 citations). She has been the principal investigator from the CSIC in two European-funded research projects in the 7FP (Multifun and NanoMag) and is participating in one FET-OPEN, HOTZYMES 2019-2021. She has also participated in other 30 national projects, has supervised 5 thesis and 1 more is on-going, and has presented more than 30 invited talks at conferences.

Chemically Engineered Iron Oxide Nanocrystals for Transport of Biomolecules Across Biological Barriers

Isabel Gessner, ShaistaIlyas, Eva Krakor, Laura Wortmann and **Sanjay Mathur**

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Chemical processing of functional ceramics has played a key role in converging disciplines, which is especially true for their bridge-building role in integrating the concepts of inorganic materials synthesis with biomedical applications. Out of a vast variety of metal and metal oxide nanoparticles that have been developed for medicinal purposes, iron oxides are one of a few materials that made it through clinical trials. Due to their high biocompatibility, stability and the abundance of iron in our environment, which results in low costs of iron-based materials, diverse iron oxide nanoparticles (IONPs) have been prepared for biomedical applications. In our workgroup, ɣ-Fe_2O_3, α-Fe_2O_3 and Fe_3O_4 based IONPs have been synthesized using a broad range of well-established synthetic procedures. By changing the reaction conditions and applying suitable surface ligands, the morphology (spherical, cube-shaped, ellipsoidal), surface charge and dispersibility of IONPs could be tuned according to the desired application allowing for a reproducible fabrication of optimized and highly efficient vectors. Controlled surface vectorization with biomolecules led to the formation of cancer targeting platforms, while the employment of the highly selective click chemistry enabled the magnetic separation of proteins out of a proteome mixture. Moreover, as-prepared particles could be used for drug delivery applications, either through covalent attachment of a drug to the particle surface or by using the IONPs as templates to prepare hollow drug containers. This talk will present how chemically grown nanoparticles can be transformed into bio-vectors for magnetic resonance imaging (MRI) and drug delivery applications.

Sanjay Mathur

Professor Sanjay Mathur is the Director of the Institute of Inorganic Chemistry at the University of Cologne in Germany. He is also the Director of the Institute of Renewable Energy Sources at the Xian Jiao Tong University, Xian, China and a World Class University Professor at the Chonbuk University in Korea. He is a Visiting Professor in the Institute of Global Innovation Research at TUAT. He also holds Visiting Professorships at the Central South University, China and National Institute of Science Education and Research, India. His research interests focus on application of nanomaterials and advanced ceramics for energy technologies. He holds ten patents and has authored/ co-authored over 430 original research publications and has edited several books. He is a Titular Member of the International Union of Pure and Applied Chemists (IUPAC) and a member of the ISO Technical Committee on Nanotechnologies. He serves as the Editor for Journal of Electroceramics, and as the Principal Editor of J. Mater. Research. He is also an Associate Editor for NanoEnergy, International Journal of Applied Ceramics Technology, International Journal of Nanoscience and Nanomaterials. He is also on the Editorial Boards of journals International Journal of Nanotechnology, Materials, Journal of

Ceramic Science and Technology. He was awarded the Honorary Doctorate of the Vilnius University in 2016. He is an Academician of the World Academy of Ceramics and Fellow of the American Ceramic Society. He also acts as the "International Ambassador" of the University of Cologne. He is the recipient of the Global Star and Bridge-Building awards of the American Ceramic Society, Lee Hsun award of the Chinese Academy of Science and Surface Innovator Award of the SSPC and AkzoNobel. He is a member of the Advisory Board of the Federation of German Materials Science (DGM) and also serves on the Board of the German Chemical Industries Network CHEMCOLOGNE. He is on the Review Advisory Panel of the CSIR, South Africa and serves as International Advisor to Korean Institute of Industrial Technology (KITECH), Incheon, Korea and Vice-President of the Thin Film Society, Singapore. He is on the ACerS Board of Directors. He has been elevated to the ASM class of fellows of 2017. He is the Chair of the Kavli Awards Subcommitee of the Materials Research Society. Since 2018, he also chairs the Academic Affairs Committee of the Materials Research Society.

Meccanotransduction of axonal growth: a new strategy based on magneticnanoparticle to romote nerve regeneration

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Axonal growth is a complex mechanism and, recently, it has been elucidated that mechanical forces play an important role. The so-called "stretch-growth model" has been proposed as an alternative to the more widely recognized "tip-growth model". According to the "stretch-growth model" elongation is induced by mechanical stimuli, whether these come from the growth cone, or originate from different stimuli such as body growth or the use of exogenous mechanical forces. However, this model is not yet accepted as a universal model of axonal growth, because some contradictions have emerged. The main one consists in the fact that some literature has highlighted the presence of a threshold value to overcome so that the mechanical force can stimulate the elongation of the axon. Nevertheless, this threshold value is higher than the tension generated at the growth cone and this is why it has been questioned if the "stretch growth model" is valid in physiological conditions. However, the tools previously used to investigate the effects of mechanical stress had limits regarding sensitivity and reliability, which makes them unusable to study tensions below 100 pN. To overcome this problem, we have labelled neuron-like cells and primary neurons by magnetic nanoparticles for the generation of a weak force, which may vary, under the action of an external magnetic field, from 0.1 to 10 pN. We demonstrate that neurite elongation proceeds at the same previously identified rate, on application of mechanical tension of ~ 1 pN, which is significantly lower than the force generated in-vivo by axons and growth cones. This observation raises the possibility that mechanical tension may act as an endogenous signal used by neurons for promoting neurite elongation.

Vittoria Raffa

Vittoria Raffa has an established international reputation by virtue of the original publications on medical aspects of nanotechnology and nanomedicine. She was author in the last 10 years of 60 publications in ISI journals (h-index 24, total citations 2200) and 5 patents on technologies relating to nanomedicine. She is Associate Professor of Molecular Biology, Ph.D. in Nanotechnology, M.Sc. in Chemical Engineering. From 2014 to 2016 she was Professor at the University of Dundee (UK) and PI of Nanobio Lab (School of Medicine, Dundee, UK). Currently, she is Professor at the University of Pisa; lecturer of 2 courses related to Molecular Biology and 2 courses related to Nanomedicine; leader the Nanomedicine Lab of the Department of Biology (UNIPI, IT). The Nanomedicine Lab is a very multidisciplinary environment, with people working at the interface of different disciplines in Life and Physical Sciences. Her long-term research interests are in the field of neuroscience and in the study of the mechanotransduction of axonal growth.

Nanomagnetic approaches for vascular healing and cardiac regeneration

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Magnetic nanoparticles and various magnet systems have been used in a range of applications aimed to achieve localized delivery of therapy and tissue regeneration. For local delivery of therapy, magnetic carriers associated with drugs, nucleic acids or loaded within cells are directed or guided by magnetic forces towards certain biological targets. The magnetic delivery of therapeutic agents results in the concentration of the therapy at the target site, consequently improving therapy delivery efficiency while reducing or eliminating the systemic therapy side effects. For tissue regeneration, magnetic nanomaterials are used in remotely controlled actuation for the release of bioactive molecules or mechanical conditioning of cells to generate tissue constructs for restorative tissue support or reconstruction. Mechanical conditioning of cells and tissue constructs is an important factor in determining the properties of the tissuebeing produced. This conditioning is particularly relevant to the generation of vascularized cardiac muscle, where mechanical stress activates mechano-sensitive receptors, triggering biochemical pathways that promote the production of functional tissue. This talk will present two applications where the magnetic approach has the potential to enable tissue restoration or support. One example will present an innovative method that takes advantage of magnetic nanoparticles and intravascular steel stents to deliver endothelial cells to the blood vessels with the ultimate aim to repair the injured artery. Another study will present a novel strategy for creating a vascularised and functional tissue graft by combining the use of a macroporous alginate scaffold impregnated with magnetically responsive nanoparticles in combination with non-invasive magneto-mechanical stimulation. While a distinct mechanism underlines the strategies described in each example, both cases demonstrate versatile capabilities of magnetic systems for regenerative applications.

Boris Polyak

Dr. Polyak earned his Ph.D. in Biotechnology Engineering in 2004 from the Ben-Gurion University, Israel specializing in biological sensors. In 2007, Dr. Polyakcompleted his postdoctoral training at the University of Pennsylvania, Children's Hospital of Philadelphia where he has been developing methods for gene and cell delivery to magnetizable implants. The goal of our group is to explore the multiple interfaces between materials science, chemistry, and life science. A major focus is on applications of magnetic phenomena in medicine, including targeted drug delivery, tissue engineering, andbioimaging. Dr. Polyak has received research and educational funding from NIH, W.W. Smith Charitable Trust, Stein Foundation, Bi-National US-Israel Science Foundation, and the State of Pennsylvania. His teaching focuses on drug delivery systems and engineering of advanced materials for regenerative applications.

Thermal therapies mediated by iron oxide-based nanoparticles: quantitative comparison of heat generation, therapeutic efficiency and limitations

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Thermal nanotherapies as magnetic hyperthermia (MHT) and photothermal therapy (PTT) are two promising emergent treatments and non-invasive approaches for tumor ablation, where localized heat generation is mediated by magnetic and photo-activatable nanomaterials[1,2]. Until very recently, these thermal nanotherapies, have been developed separately: MHT is mainly focused on the use of magnetic iron oxide nanoparticles due to their excellent biodegradability[3], while metallic nanoparticles such as gold nanomaterials are often preferred due to their strong absorption cross sections. They have recently begun to intersect due to the recent discovery and use of photothermal properties of iron oxide nanostructures[4] or to the use of magneto-photothermal hybrids[5], which efficiently combine both heating features in one-single object.

A comprehensive comparison of the heating efficiency of magneto- versus photo-thermal effect is presented, where different magnetic nanoparticles have been confronted (iron oxides, cobalt ferrite, spheres, cubes, flowers) with different metallic nanoparticles in aqueous, cellular, and tumoral environment[6]. Intracellular processing markedly impacted MHT, while endosomal sequestration could have a positive effect for PTT. In the search for the most therapeutically viable modality, the effect of nanoparticle concentration and the experimental exposure parameters (magnetic field strengths/frequencies and laser power densities) have been investigated. The intracellular biotransformations of these nanomaterials in the biological environment has also been explored through the study of their physical and chemical modifications at the nanoscale over the time[7].

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Ana Espinosa

After obtaining a PhD in the domain of wide band gap oxides for applications in Information Technologies in 2010, AE worked as a postdoctoral fellow at the Magnetism and Magnetotransport Laboratory (ICMM-CSIC, Spain) on the study of structural and magnetic properties of nanoparticle systems. In 2013, she joined the Laboratoire de Matière et Systèmes Complexes (MSC, France) to conduct a research activity based on nanotherapies for cancer treatment by means of thermal effect (magnetic and plasmonic hyperthermia) as an Intraeuropean Marie Curie postdoctoral fellow. In 2017, she moved to the Materials for Health group (CSIC, Spain) with the aim of studying different synthesis protocols of nanostructures for magnetic nanotherapies. Recently, AE has joined the IMDEA Nanoscience (Spain) research center to study multifunctional strategies based on magnetic and photothermal nanoplatforms for cancer treatment.

On the feasibility of improving heat production in magnetic fluid hyperthermia: the time of topology

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The use of magnetic nanoparticles (MNPs) as nanosized sources of intracellular heat to fight cancer, a therapy known as Magnetic Fluid Hyperthermia (MFH), relies on the capacity of MNPs to heat cancer cells up to temperatures of 42-46ºC by a remote radiofrequency magnetic field. Although already applied in clinical protocols, there is still a lot of room in MFH to further improve the heating efficiency, a desirable goal in order to lower the administered doses of MNPs while keeping their therapeutic efficacy. It has become clear along the last years that under physiological conditions, the power absorption is hindered by different effects like agglomeration, changes in local viscosity and pH within the cell, attachment to membranes, etc. Quite a lot of effort has been applied to understand how each one of these impairments can be overcome and make the MNPs to heat regardless of their physicochemical environment. The formation of low-dimensionality arrangements of single-domain MNPs is being considered lately as a possible way to use magnetic dipolar interactions to increase the power absorption by Néel relaxation. It has been reported that linear structures such as elongated clusters or chains can raise the values of the specific power absorption of MNPs. These structures have been theoretically modeled and it is now apparent that new magnetic phenomena are in place and require unequivocal experimental data in order to understand the complex magnetism of these systems. Our recent work addressed the issue of how agglomeration of MNPs *in vitro* affects the heating efficiency, and how the induced formation of low dimensional structures can improve it. We have observed that systematic data from naturally agglomerated MNPs in gel and resin phantoms can be compared to well-characterized clusters formed within the cytoplasm of cultured cells. We found clear evidence that MNPs clusters grown under DC applied fields have lower fractal dimension than the corresponding control cells, and the resulting heating rates increased both in synthetic phantoms and within cells. The experimental data and numerical modelling support the idea that magnetic dipolar interactions can be maneuvered to increase the effective heating efficiency of the MNPs within cells.

Gerardo F. Goya

Dr. Gerardo F. Goya (Argentina, April 1964) completed his PhD degree at the University of La Plata and Centro Atómico Bariloche, Argentina. During 2001-2007 Prof. Goya has been Associate Professor at the Institute of Physics, University of Sao Paulo (Brazil), where he created and managed the mechanochemistry laboratory at the Materials Physics Department (DFMT).
Dr. Goya is currently Associate Professor at the University of Zaragoza, Spain, where he joined the Institute of Nanoscience of Aragón (INA) in 2005 to start and consolidate a new research line on nanomagnetism and biomedical applications of magnetic nanoparticles, mainly magnetic hyperthermia. The achievements in this period include new methods of synthesis of magnetic NPs with improved control of size and magnetic properties, and the successful proof of principle of a 'Trojan Horse strategy' for oncology, by inducing cell death with magnetic hyperthermia in dendritic-cell primary cultures. In addition, the group has developed several studies of different biological agents as models of interaction with magnetic particles. Prof. Goya led the design, development and building of a unique equipment for measuring power absorption in magnetic hyperthermia. This was a pioneer system with many technological improvements designed to make a fully automatic measuring system. The innovation of these activities made the basis for a spin off company from the University of Zaragoza, of which he is co-founder and scientific advisor. He has more than 150 international publications (h-index=36) with more than 5000 citations, 2 PCT patents and more than 120 conference presentations including more than 40 invited talks. His work has established an internationally recognized research group in biomedical applications of magnetic nanoparticles, composed of engineers, biologists, chemists, and physicists. In collaboration with top-level parasitologists, immunologists and medical doctors, the group has managed to consolidate a common platform in biomedicine, which is reflected in the coordination of highly innovative multinational projects.

Graphene oxide functional nanohybrids with magnetic nanoparticles for improved vectorization of anticancer therapeutics

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Nanographene Oxide (NGO) due to the hexagonal sp^2-bonded carbon atoms lattices structure, possessed superior electrical, chemical, physical, mechanical, and biological properties making them attracting materials for the fabrication of highly engineered hybrid nanocarriers. Such materials, resulting from the combination with polymers from both synthetic and natural origin, are receiving increasing attention in biomedicine. We recently proved that the functionalization of the polymer counterpart with polyphenol compounds is a valuable strategy to obtain of a functional drug delivery system, in which the biological effect is related to both the loaded drug and the carrier itself. A further improvement was achieved by functionalization with magnetic nanoparticles, with the possibility to target the payload at the proper site. In this presentation, we combined graphene oxide, iron oxide nanoparticles, and a newly synthesized human serum albumin–curcumin conjugate for the fabrication of a multifunctional nanohybrid to spatially control the vectorization of doxorubicin to neuroblastoma SH-SY5Y cells. Each component contributed to the performance of the final nanohybrid: (1) magnetic nanoparticles act as a targeting element; (2) NGO enhances the drug loading capability and makes the release profile prolonged over time; and (3) immobilized curcumin in the functional coating synergizes the drug cytotoxicity. The effectiveness of the proposed system is tested by a multidisciplinary approach, which combines expertise in materials science, chemistry, biology, and oncology.

Giuseppe Cirillo

Giuseppe Cirillo (Italy, June 1980) completed his PhD degree in 2008 and currently works in the fields of Materials Science, Pharmaceutical Technology and Macromolecular Chemistry at Department of Pharmacy, Health and Nutritional Sciences, University of Calabria (Italy). The interest in nanomedicine was implemented during the post-doctoral fellowships at University of Calabria from 2009 to 2016 in cooperation with IFW Dresden where he was visiting researcher. During this period, further cooperation were established at an international level focusing on the development of polymer therapeutics and multi-functional hybrid materials for biomedical and pharmaceutical applications. He has more than 100 publicationsin ISI journals (h-index=30, total citations 2500). He achieved the National Qualification as Associate Professor in Drug technology, socioeconomics and regulation and in the Chemical basis of Technology Applications in 2012 and 2016. He was lectures on Chemistry and Biochemistry of Fermentations; Innovative Drug Delivery Devices; and Pharmaceutical Technology.

Engineering and optimization of Specific Absorption Rates of Fe oxidenanoparticles in magnetic hyperthermia

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Issues related to the magnetic response of complex systems consisting of different types of Fe oxide nanoparticles (with different shapes and aspect rations, non-interacting or forming assembles, etc.) with respect to magnetic hyperthermia effects are emphasized together with proposed theoretical and experimental solving items. Specific characterization methodologies based on temperature and field dependent Mössbauer spectroscopy and SQUID magnetometry deserving an adequate magnetic characterization of the nanoparticulate systems in respect to phase composition, local and long-range magnetic structure, intra- and inter-particle magnetic interactions and mainly to the magnetic relaxation phenomena of interest for heat transfer mechanisms in magnetic hyperthermia are underlined. The different methodologies for the correct evaluation of the specific absorption rate (SAR) from real experimental data taking into account also environmental loss factors are critically discussed. Micromagnetic simulations and complementary analytical tools are used in order to search for optimal shapes and sizes of non-interacting Fe oxide magnetic nanoparticles leading to enhanced specific absorption rates. A specific attention is provided to the effects of inter-particle (dipolar type) interactions on the magnetic relaxation effects in magnetic fluids of different volume fractions. It has been proven by micromagnetic simulations that the direct effect of the inter-particle dipolar interaction is not only an increased particle anisotropy energy but also a decrease of the characteristic time constant τ_0, with direct influence on the efficiency of the heat transfer during potential hyperthermia treatments. Experimental determination of specific absorption rates on ferrofluids with similar nanoparticles but of different volume fractions as well as in case of ferrofluids with different shapes and size of nanoparticles are presented and discussed.

Victor Kuncser

Dr Victor Kuncser, is currently a Research Professor at The National Institute of Materials Physics in Bucharest-Magurele (http://www.infim.ro), Head of the Magnetism and Superconductivity Department and a member of the executive board of the Institute. He is PhD promoter as Professor associated to University of Bucharest, Faculty of Physics.His previous appointments and research secondments include: Rostock and Duisburg Universities, University of Rouen, Padova and Zaragoza, Deutsche Synchrotron and Berlin Neutron Scattering Center. Victor received his PhD in Physics in 1995 at the Institute of Atomic Physics, Bucharest-Magurele and has been awarded the Alexander von Humboldt fellowship in

2001 and the prize of the Romanian Academy in 2002. Victor published more than 200 scientific papers in ISI quoted international journals, six book chapters and was coeditor of a Springer book. His scientific interest is in the field of magnetic interactions and local phenomena in intermetallics and oxides, molecular magnets, ferrofluids, magnetic nanocomposites, multifunctional and magnetofunctional materials, thin films and multilayers.

Taking magnetic hyperthermia and magnetogenetics to the next level: key aspects to address from a basic-physics point of view

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The aim of the talk is to highlight some key aspects that, in my opinion and from the theoretical point of view, need to be addressed in order to achieve further biomedical success using the heat released by nanomagnets under AC fields: despite the promising application perspectives (hyperthermia cancer treatment; drug release; magnetogenetics; etc.), the fact is that the success in reaching routine clinical practice is very scarce. From the physics point of view, a main difficulty is the lack of theoretical models able to describe the behaviour of MNPs in the viscous biological environment, what results in the absence of accurate tools able to guide the experiments. The failure in the current models involves several key factors, including procedural (complete impossibility to explain successful heating effects on cells when the global heating is negligible); interpretative (current heating mechanisms cannot account for accurate heat-triggering experiments – other mechanisms at play?); and descriptive ones (available models are limited to short timescales, far from those of the experiments). The complex nature of the problem requires a multiphysics approach to go beyond the state-of-of-the art and overcome the above limitations, able to; simultaneously embrace superparamagnetic and Brownian processes; provide alternatives to current heat generation mechanisms; and efficiently deal with the different timescales involved. During the talk I will try to summarize the limitations and a possible approach to overcome them, with the objective of developing of a general framework for the comprehension of the heating performance of magnetic nanoparticles under AC magnetic fields in viscous media.

David Serantes

David Serantes currently holds a combined teaching and research position at the Universidade de Santiago de Compostela (USC) in Galicia, Spain. His expertise is on theoretical nanomagnetism, being his research characterized by a strong interaction with experimentalists. He obtained his PhD on magnetocaloric properties in nanosystems at the USC in 2011; then as a postdoc he joined the ICMM (Madrid, Spain) to work on ultrafast magnetisation dynamics. Since then, his work is focused on the study of magnetic nanoparticles for biomedical applications. Particularly, he studies their response under external AC fields to be used as heat mediators for biomedical applications, as hyperthermia cancer treatment (second postdoc at the University of York, UK) or the remote magnetogenetic control of cellular activities (core of his current project). His investigation involves the development of new theoretical models, requiring the combination of the multi-scale atomistic-to-macrospin approximation with the (mechanical) Brownian dynamics (rotation, displacement), which were traditionally considered separate areas of knowledge.